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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/527,925	09/15/2005	Raymond John Steptoe	18749	8585

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/527,925	STEPTOE ET AL.	
	Examiner	Art Unit	
	Q. JANICE LI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/19/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment and response filed 12/19/07 are acknowledged. Claim 1 has been amended. Claims 18-25 have been canceled. Claims 1-17 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 12/19/07 response would be addressed to the extent that they apply to current rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8, 10, 12-16 stand rejected under 35 U.S.C. 103(a) as being unpatentable over *Bochan et al* (Transplant proc 1999;31:690-1), in view of *Burt et al* (Autoimmunity Rev 2002;1:133-8), for reasons of record and following.

Bochan et al teach a method for treating insulin-dependent diabetes in a subject comprising collecting a sample of hematopoetic stem cells from the bone marrow of the rat, infecting the HSCs with a recombinant AAV vector expressing rat proinsulin, and reintroducing the transfected HSCs to rats with STZ-induced diabetes. *Bochan et al* reported transgene expression in several tissues of the rat, and the expression lasted for up to 6 wks, and in the short term, they were able to reverse STZ-induced diabetes (e.g. figs and page 691).

Although *Bochan et al* do not specify whether the HSCs injected to STZ-diabetic rats are autologous, this is known in the art as taught by *Burt et al* (§ 4). Although *Bochan et al* conducted the experiment in rat, and used rat proinsulin II, it is clear the investigation was a feasibility study for treating diabetes in humans.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by *Bochan et al,* in treating human diabetes upon completion of necessary pre-clinical studies and use autologous HSCs and human insulin in a human subject, with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the ultimate goal of animal study is to develop a treatment strategy for treating human diabetes. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

In the remarks, the applicant states, "the present invention is partly predicated on the recognition that transplantation of syngeneic or autologous HSCs infected with proinsulin can induce immune tolerance" and "Burt et al. merely mention that autologous HSC transplants, in contrast to allogenic HSC transplants, are relatively safe".

In response to applicant's argument that applicant recognizes a different mechanism for using autologous cells, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art

cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

In the instant case, mere mention of the preference of autologous over allogeneic HSCs is sufficient to illustrate the state of the art. In the newly submitted post-filing reference by the applicant (exhibit I), *Burt* again states, "HEMATOPOIEITIC STEM CELL TRANSPLANTATION FOR THE TREATMENT OF AUTOIMMUNE DISEASES HAS BEEN OVERWHELMINGLY AUTOLOGOUS" (1st zpar of col 1, page 2466), which provides further support to confirm the state of the art at the instant filing date.

The applicant then asserted that autologous transplantation strategy was yet to be tested in the treatment of diabetes, citing a post-filing publication by *Burt*, (2004) showing that allogeneic, but not autologous, transplantation resulted in marked amelioration of rheumatoid arthritis.

The argument and exhibit has been fully considered but found not persuasive to obviate instant rejection for the following reasons:

1) The knowledge reflected in the post-filing application was not available at the time of instant filing date, hence using autologous HSCs would have been obvious and had been overwhelmingly used by the ordinary skilled in the art.

2). The applicant's disclosure embraces both autologous and allogeneic sources of HSCs because the specification states "The process of the present invention may be "syngeneic", "allogeneic" or "xenogeneic" with respect to the subjects within an animal species from which HSCs and/or HPCs are isolated and the subjects who receive the cells… Preferably, the method of the present invention is conducted as a syngeneic process. To the extent that

either an allogeneic or xenogeneic process is utilized, it should be understood that it may be necessary to modify the protocol such that any immunological responses, which may occur due to the mixing of foreign immuno-competent cells, are minimised" (Specification, paragraph 0040);

3). It appears by citing *Burt* 2004 reference and several other references (exhibits 2-3), the applicant admits on record that the claimed method was not sufficiently tested and hence not fully enabled at the time of the filing date. These references raise doubt on the enablement of the claimed invention, but the knowledge that become available after instant filing date does not obviate the obviousness at the time of instant priority date.

Accordingly, the rejection stands.

Claim 11 stands rejected under 35 U.S.C. 103(a) as being unpatentable over *Bochan et al* (Transplant proc 1999;31:690-1), in view of *Burt et al* (Autoimmunity Rev 2002;1:133-8) as applied to claims 1-8, 10, 12-16 above, further in view of *Slavin et al* (USP 6428782), for reasons of record and *supra*.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 17 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and following.

The applicant indicated in the Remarks, claim 9 and 17 will be canceled. However, this is not the case.

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is **571-272-0730**.

The examiner can normally be reached on 9:30 am - 7:30 p.m., Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

For all other customer support, please call the USPTO Call Center (UCC) at **800-786-9199**.

/Q. JANICE LI, M.D./
Primary Examiner, Art Unit 1633

QJL
April 1, 2008